REMARKS/ARGUMENTS

In response to the Office Action of January 16, 2007, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim Status/Support for Amendments

New claims 15-17 have been further amended. Claims 1-4 have been cancelled. Claims 13 and 14 were cancelled in a previous response (filed on June 27, 2005). Claims 5-12 are withdrawn from consideration. It is understood that claims 5-12, drawn to the non-elected invention, will remain pending, albeit withdrawn from consideration on the merits at this time. Applicants wish to preserve their right to present claims 5-12 in a divisional application(s).

Rejections under 35 USC 112, first paragraph

The rejection of claims 1-4 under 35 USC § 112, first paragraph, as set forth at ¶ 6 of the previous office action (01/04/2006) has been maintained for reasons of record insofar as it is applied to new claims 15-17, which replace canceled claims 1-4.

Claims 15-17 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detection of thrombospondin, is alleged by the Examiner to not reasonably provide enablement for diagnosis of Alzheimer's dementia via detection of a thrombospondin polypeptide in a body fluid sample from a mammal. The specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Further amended claims 15-17 are now drawn to a method for diagnosing Alzheimer's dementia in a human patient suspected of suffering from Alzheimer's disease, determining a presence of a thrombospondin polypeptide in a body fluid sample from said human patient by contacting the sample with at least one antibody which specifically binds to a thrombospondin polypeptide weighing about 180 kDa, wherein the presence of said thrombospondin polypeptide is diagnostic for Alzheimer's dementia.

The Examiner acknowledges that the newly submitted Figure 2 resolves the previous issue surrounding that figure, however the rejection is nevertheless maintained because it remains the Examiner's position that the presence of thrombospondin (TSP-1) may be detected in patients for other conditions, such as

ischemic/reperfusion injury following MI. Therefore the Examiner contends that such a test would not be definitive for AD.

The claims have now been amended such that the process is directed towards a method for diagnosing Alzheimer's dementia in a human patient suspected of suffering from Alzheimer's dementia comprising (a) contacting a sample of a body fluid obtained from said patient with at least one antibody which specifically binds to a thrombospondin polypeptide weighing about 180 kDa; and (b) determining a presence of said thrombospondin polypeptide in said sample; wherein the presence of said thrombospondin polypeptide is diagnostic for Alzheimer's dementia.

It is respectfully submitted that by selecting a suspect patient population (as now required by the clims), the utility demonstrated in the specification is evident. In this patient population, determination of the presence of the 180 kDa thrombospondin polypeptide would be definitive of AD, and thereby obviate the rejection.

Rejection Under 35 USC 102(e):

The rejection of claims 1-4 under 35 USC § 102(e), as set forth at paragraph 11 of the previous office action (01/04/2006) has been maintained for reasons of record insofar as it is applied to new claims 15-17, which replace canceled claims 1-4.

Newly added claims 15-17 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,605,592, to Ni et al. or in the alternative US PGPub 20020068319 by Ni et at., as evidenced by Asakura et al. (J. Neuroimmunol. 1996; 65:11-19). The Ni et al. references are cumulative and are therefore cited together with identical reasoning therefore.

At page 18 of the response filed July 10, 2006, Applicants have previously asserted that Ni et al. does not teach a thrombospondin peptide, but a peptide that shares some similar domains with thrombospondin. Applicants further argue that even if Ni et al. did disclose thrombospondin, they do not teach a polypeptide subunit of thrombospondin-1 weighing about 180 kDa that was identified as present in Alzheimer's patients and absent in control patients and thus useful as a marker for diagnosing Alzheimer's disease. Applicants have thus asserted that Ni et al. cannot be said to either expressly or inherently describe each and every element in the claims as now presented for examination.

Applicants' arguments have been fully considered by the Examiner, however they are not deemed to be persuasive. Ni et al. teach a novel THRAP protein that exhibits 13 thrombospondin-1 (TSP-1)-like domains, IgG-like domains and proteinase inhibitor-like domains, as in Figure 4. It is also noted that Figure 5 of the patent shows the regions of identity between the amino acid

sequence of THRAP and the translation product of thrombospondin-like protein as determined by BLAST analysis. Further, Ni et at. disclose that the predicted molecular weight of the THRAP protein is about 191 kDa (see column 24, lines 46-47), which is "about 180 kDa" as instantly recited. Thus, the Examiner alleges that the THRAP protein disclosed by Ni et al. bears striking homology to TSP-1, both in terms of its amino acid sequence and its predicted weight, and would thus meet the limitation of "a thrombospondin polypeptide weighing about 180 kDa." The takes the position that the recitation of the molecular weight in the claims is not meaningful, and Ni fully anticipates this limitation. Moreover, the Examiner asserts that Ni et al. teach an analysis of the THRAP amino acid sequence (Figure 6), with highly antigenic regions of the THRAP protein identified, i.e., regions from which epitope-bearing peptides of the invention can be obtained.

New claims 15-17 recite a method for diagnosing Alzheimer's dementia comprising contacting a sample of a body fluid with at least one antibody which specifically binds to a thrombospondin polypeptide weighing about 180 kDa and determining the presence of said thrombospondin polypeptide in said sample.

The Examiner then posits that the diagnostic method thus hinges on the specificity of the antibody for binding to a

thrombospondin polypeptide in order to detect the polypeptide's presence, and that because of the tremendous overlap in amino acid sequence and antigenic epitopes between the THRAP protein disclosed by Ni and the thrombospondin protein, it would be expected that the antibodies disclosed by Ni for detection of THRAP protein and diagnosis of Alzheimer's disease would be capable of detecting thrombospondin and diagnosing Alzheimer's dementia as instantly claimed.

The Examiner grounds this theory on the basis that antibodies, even monoclonal antibodies, are notoriously promiscuous in terms of their capacity to bind similar epitopes on different proteins. Finally, as noted in the previous office action, the Examiner reiterates that Ni et al. teach that the protein may be detected in bodily fluids such as lymph, serum, plasma, urine, synovial fluid and spinal fluid, taken from an individual having the disorder and compared to a sample from an individual not having the disorder. Additionally, Ni et al. disclose various immunoassay techniques for detecting a polypeptide of the invention, including, but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassay, ELISA, "sandwich" immunoassays, western blots, precipitation reactions, etc. (see column 186, lines 45-67). Ni et al. teach that detection of THRAP polypeptide and/or

fragments thereof in a biological sample is useful for the diagnosis of Alzheimer's disease (see column 91, lines 27-37). Accordingly, the Examiner concludes that the teachings of Ni et al. anticipate instant claims 15-17.

Applicants strongly disagree with the position taken by the Examiner. Contrary to the Examiner's assertions, THRAP is simply not equivalent to thrombospondin, the claimed molecular weight of about 180 (as established via gel electrophoresis) is, in fact, different from the "about 190" of Ni et al, and it is well-established that any changes to the sequence of a peptide may very well have a substantial effect on binding, and therefore the ability of a diagnostic assay to function with the degree of sensitivity and specificity required.

If a rejection is maintained under 35 USC 102, it is given to mean that every limitation of the claim is set forth in the reference. This would not seem to be the case here. Alternatively, perhaps the Examiner is alleging "inherency" as a means of rationalizing maintaining the Ni et al disclosure as anticipatory of the claimed invention. It is respectfully submitted that such a presumption of inherency is not sufficient for maintenance of a rejection under 35 USC 102.

Given the known unpredictability of the art and the degree of experimentation required to ascertain such facts as the

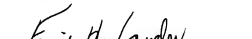
Examiner alleges, it is respectfully submitted that the propriety of such a rejection must fail based upon a review of the Wands factors. In all due respect to the Examiner, the allegation of anticipation over Ni is simply not justified and is certainly not supported by any factual underpinnings sufficient to constitute anticipation within the meaning of 35 USC 102. The identification of a unique protein "THRAP" in the '592 patent as an angiogenesis regulating protein which shares regions of identity with the translation product of "thrombospondin-like protein" would seem to be a far cry from a teaching that THRAP is equivalent to the thrombospondin peptide of the instant invention. Certainly it can not be determined that the THRAP protein of the '592 having a predicted molecular weight of about 191, is anticipatory of the claimed "about 180 kda" peptide of the instant claims, and has the same physiological activity a relative to Alzheimer's disease, binding characteristics, etc. thereof.

For these reasons it is respectfully requested that the rejection over Ni et al be withdrawn.

CONCLUSION

In light of the foregoing remarks and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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